

Application No. 09/871,227  
Amendment Dated September 22, 2003  
Reply to Office Action of April 25, 2003  
and Advisory Action of August 1, 2003  
Docket No. 1256-00765

### **REMARKS**

In the Office Action dated April 25, 2003, claims 1-56 were examined with the result that all claims were rejected. The Examiner made the rejection final. In response, Applicant herein files a Request for Continuing Examination and submits a Declaration of Hector F. DeLuca, one of the named inventors. In view of the following remarks, reconsideration of this application is requested.

In the Office Action, the Examiner essentially had two categorical claim rejections. The first was under the doctrine of obvious type double patenting, and the second was a §103(a) obviousness rejection. Before dealing with the double patenting rejections, Applicant would like to deal with the §103(a) rejections as follows.

### **35 USC§103(a) REJECTIONS**

In the Office Action, the Examiner rejected claims 1-4 and 9-32 under 35 USC §103(a) as being unpatentable over DeLuca et al U.S. Patent 5,945,410. The Examiner stated that the DeLuca et al '410 patent teaches a generic group of 2-alkyl-19-nor-vitamin D compounds and exemplifies in particular 2-methyl-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>. Thus, since the compounds disclosed in the '410 reference are adjacent lower homologs of the instantly claimed compounds, the Examiner concluded that this close structural similarity rendered the instantly claimed 2-ethyl compounds obvious.

Also in the Office Action, claims 5-8 and 33-56 were rejected under 35 USC §103(a) as being unpatentable over DeLuca et al U.S. Patent 5,843,928. The Examiner stated that the DeLuca et al '928 reference teaches a generic group of 2-alkylidene-19-nor-vitamin D compounds and exemplifies in particular 2-methylene-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>. Accordingly, since the compounds disclosed in the '928 reference were adjacent lower homologs of the instantly claimed compounds, the Examiner concluded that this close structural similarity rendered the instantly claimed 2-ethylidene compounds obvious.

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In response to the above rejections, Applicant submitted an indirect comparison of the claimed compounds versus the prior art compounds disclosed in the above two references. Applicant did this by comparing the intestinal calcium transport activity and the bone calcium mobilization activity data disclosed in the '410 and '928 references with the intestinal calcium transport activity and the bone calcium mobilization activity data disclosed in Applicant's specification. Based on this indirect comparison, Applicant showed that the biological activities of the instantly claimed compounds were significantly different from those of the prior art compounds. The Examiner, however, rejected Applicant's indirect comparison indicating that this comparison was not a true side-by-side comparison. The Examiner concluded that since the comparison was not a true side-by-side comparison, it did not refute the prima facie case of obviousness set forth by the Examiner. Accordingly, the Examiner made the rejection final.

In response to the final rejection, Applicant submitted further remarks in an Amendment dated July 16, 2003 which attempted to further explain the indirect comparison to the Examiner. However, the Examiner issued an Advisory Action dated August 1, 2003 indicating that the request for reconsideration had been considered but still did not place the application in condition for allowance. Once again, the Examiner requested a side-by-side comparison of compounds that differ only in the substituent at the 2-position under identical conditions.

In response, Applicant has now filed a request for continuing examination, and submitted a Declaration of Hector F. DeLuca which accompanies these remarks. The Examiner will see in the DeLuca Declaration that Applicant has compared compounds that differ only in the substituent at the 2-position. Thus, for example, in paragraph 11 of the DeLuca Declaration, there is set forth a comparison of 2 $\alpha$ -methyl-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> versus 2 $\alpha$ -ethyl-19-nor-1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>. As the Examiner can see, the enclosed DeLuca Declaration supports and reconfirms the indirect comparison previously presented in this case. Thus, Applicant believes that it has adequately shown via the enclosed DeLuca Declaration that Applicant's compounds have

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distinct biological activity from the prior art compounds of the DeLuca et al '410 patent and the DeLuca et al '928 patent. The DeLuca Declaration provides a side-by-side analysis of the biological activity of these compounds and supports the conclusion that, even though the instantly claimed compounds are structurally similar to the prior art compounds of the '410 and '928 patents, the biological activities of Applicant's instantly claimed compounds are different and unexpected as compared to the prior art compounds. Applicant believes the enclosed DeLuca Declaration is persuasive and provides adequate probative evidence of nonobviousness.

As a result, Applicant believes the Examiner should withdraw the rejection of claims 1-56 under 35 USC§103(a).

#### OBVIOUSNESS TYPE DOUBLE PATENTING

In the Office Action, the Examiner rejected claims 1-4 and 9-32 under the doctrine of obviousness type double patenting as being unpatentable over claims 1, 2, 7 and 12-20 of the '410 reference. The Examiner indicated that since the present application claimed a homolog of the compound exemplified in the '410 patent, it would be expected that homologs would have the same properties and thus have similar uses as taught by the '410 reference.

However, as discussed previously herein, and as shown in the DeLuca Declaration which accompanies these remarks, the compounds of claims 1-4 and 9-32 do not have the same properties as the compounds claimed in the '410 patent. Thus, as stated by the Examiner, since the compounds of claims 1-4 are homologs of the compounds disclosed in the '410 patent, one would expect their activities to be substantially the same.

However, as noted herein and as shown in the DeLuca Declaration, these activities are not substantially the same, resulting in the compounds of claims 1-4 not being obvious in view of the compounds disclosed in the '410 patent. Thus, Applicant requests the Examiner withdraw the obviousness type double patenting rejection of claims 1-4 and 9-32.

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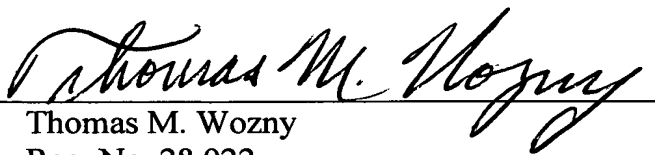
In the Office Action, the Examiner rejected claims 5-8 and 33-56 under the doctrine of obviousness type double patenting as being unpatentable over claims 1, 2, 7 and 12-16 of the '928 reference. The Examiner indicated that since the present application claimed a homolog of the compound exemplified in the '928 patent, it would be expected that the homologs would have the same properties and thus similar uses as taught by the '928 reference.

However, as discussed previously herein, and as shown by the DeLuca Declaration accompanying these remarks, the compounds of claims 5-8 and 33-56 do not have the same properties as the compounds claimed in the '928 patent. Thus, as stated by the Examiner, since the compounds of claims 5-8 are homologs of the compounds disclosed in the '928 patent, one would expect their activities to be substantially the same. However, as noted above, and as illustrated by the enclosed DeLuca Declaration, these activities are not substantially the same resulting in the compounds of claims 5-8 not being obvious in view of the compounds disclosed in the '928 patent. Thus, Applicant requests the Examiner withdraw the obviousness type double patenting rejection of claims 5-8 and 33-56.

An effort has been made to place this application in condition for allowance and such action is earnestly requested.

Respectfully submitted,

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